IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.,	)	
Plaintiff,	)	C.A. No. 17-275 (LPS) C.A. No. 17-1353 (LPS)
v.	)	
OXFORD NANOPORE TECHNOLOGIES, INC. and OXFORD NANOPORE TECHNOLOGIES, LTD.,	)	[redacted] REDACTED - PUBLIC VERSION
Defendants.	)	

DEFENDANTS' OPENING BRIEF IN SUPPORT OF ITS MOTION FOR SUMMARY JUDGMENT

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November 22, 2019

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I. NATURE AND STAGE OF THE PROCEEDINGS

Plaintiff Pacific Biosciences of California, Inc. ("PacBio") filed a patent infringement action against Defendants Oxford Nanopore Technologies, Inc. and Oxford Nanopore Technologies, Ltd. ("ONT") on March 15, 2017, and has alleged infringement of U.S. Patent Nos. 9,546,400 (the "'400 Patent") [Ex. V1], 9,772,323 (the "'323 Patent") [Ex. V2], 9,738,929 (the "'929 Patent") [Ex. V3], and 9,678,056 (the "'056 Patent") [Ex. V4].

The Court issued its Claim Construction Order (D.I. 153) and Memorandum Opinion (D.I. 154) on March 6, 2019. Fact and expert discovery is complete. Pursuant to the Court's Amended Scheduling Order (D.I. 328), dated September 6, 2019, a hearing on case dispositive motions is set for January 7, 2020 at 11:00 am, and trial is set for March 9, 2020.[1] ONT now moves for summary judgment under Fed. R. Civ. P. 56 that: (i) the '056 Patent is invalid as indefinite or lacking enablement, (ii) the accused products do not infringe the '400 and '323 Patents to the extent they use the [redacted] algorithm, (iii) ONT's [redacted] has not infringed the '929 Patent, and (iv) certain prior art references were publicly available under 35 U.S.C. § 102.

II. SUMMARY OF THE ARGUMENT AND STATEMENTS OF FACTS

The '056 Patent is invalid on at least two grounds. As the Court held in its *Markman* ruling, the '056 Claims are indefinite because a person of skill in the art cannot ascertain whether a translocating enzyme "exhibits two kinetic steps" having rate constants within the claimed ratios. Enzymes have a virtually limitless number of different enzymatic schemes and steps, and one of skill in the art has no way to know which steps to use to assess infringement of the '056 Claims. Further expert discovery, including PacBio's suggested reliance on the dwell time distribution that an enzyme "exhibits", has not resolved this ambiguity. Additionally, the '056 Patent does not enable one of skill in the art to select an enzyme and reaction conditions that would exhibit kinetic steps

[1] All docket entry numbers are to case number 17-275-LPS unless otherwise noted.

having rate constants within the claimed ratio from the myriad of existing translocating enzymes, mutations of those enzymes, and reaction conditions that may be applied.

While ONT disputes that any of its accused products infringe the '400, '323, and '929 Patents, for certain products, PacBio has provided no evidence of infringement at all. PacBio has not—and cannot – produce evidence sufficient to show that ONT's newest basecallers using the [redacted] compare a measured property with the claimed "calibration information" in the '400 and '323 Claims. Moreover, there is no evidence that the [redacted] product accused by PacBio was ever sold or used in the U.S. Finally, undisputed evidence establishes that the Winters-Hilt Grant, the Akeson Grant, and their respective progress reports were publicly available before the '400 and '323 Patents' priority date; as such, they qualify as prior art under 35 U.S.C. § 102.

The facts relevant to each of these issues are stated in the sections below.

III. LEGAL STANDARD FOR SUMMARY JUDGMENT

Summary judgment is appropriate when "the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). A genuine material fact dispute exists only if "a reasonable jury could return a verdict for the nonmoving party." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248 (1986). As emphasized by the Federal Circuit, "summary judgment... is entirely appropriate, in a patent as in any other case." *SRI Int'l v. Matsushita Elec. Corp. of Am.*, 775 F.2d 1107, 1116 (Fed. Cir. 1985) (en banc).

IV. ARGUMENT

A. The '056 Patent is Invalid Because the Claims are Indefinite and Not Enabled.

1. Legal Standards for Indefiniteness and Enablement

Indefiniteness is a question of law. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 789 F.3d 1335, 1337 (Fed. Cir. 2015). "[A] patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable

certainty, those skilled in the art about the scope of the invention." *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120, 2124 (2014). A claim is indefinite if a person of ordinary skill in the art ("POSA") cannot be reasonably certain of the scope of the claim. *Teva*, 789 F.3d at 1344–45 (different methods of measuring the claimed polymer weight provided different results); *Dow Chem Co. v. Nova Chem Corp.*, 803 F.3d 620, 633–35 (Fed. Cir. 2015) ("four methods may produce different results" for calculating claimed scope of strain hardening).

Enablement is a question of law based on underlying factual findings. *MagSil Corp. v. Hitachi Glob. Storage Techs., Inc.*, 687 F.3d 1377, 1380 (Fed. Cir. 2012). The specification must enable a POSA to make and use the claimed invention. 35 U.S.C. § 112, ¶ 1. "Claims are not enabled when, at the effective filing date of the patent, one of ordinary skill in the art could not practice their full scope without undue experimentation." *Wyeth & Cordis Corp. v. Abbot Labs.*, 720 F.3d 1380, 1384 (Fed. Cir. 2013) (affirming summary judgment because synthesizing and screening tens of thousands of compounds to practice the full scope of the claims required undue experimentation). Undue experimentation is determined by weighing the *Wands* factors: (1) the scope of the claimed invention; (2) the nature and predictability of the field; (3) the quantity of experimentation necessary; (4) how routine any necessary experimentation is in the relevant field; (5) the amount of guidance presented in the patent; (6) whether the patent discloses specific working examples of the claimed invention; and (7) the level of ordinary skill). *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988); *Idenix Pharms. LLC. v. Gilead Sciences Inc.*, 2019 WL 5583543 at *3 (Fed. Cir. Oct. 30, 2019). "[A]n iterative, trial-and-error process" may establish undue experimentation to support a finding of non-enablement. *ALZA Corp. v. Andrx Pharm., LLC*, 603 F.3d 935, 941 (Fed. Cir. 2010). A patentee cannot rely solely on the knowledge of a person of ordinary skill to serve as a substitute for information missing from the specification needed to enable the invention. *Id.*

2. Statement of Facts Relating to the '056 Patent

a. *Translocating enzymes are diverse in both structure and function, and translocating enzyme kinetics cannot be predicted without testing.*

A translocating enzyme, as that term is understood by a POSA, may be any enzyme that translocates along a nucleic acid. Ex. V5, McHenry Tr. at 80:22–81:6; *see also* Ha Decl. at ¶ 154. An enormous number of different translocating enzymes exist in nature. *See*, *e.g.*, Ex. V5, McHenry Tr. at 53:15–16; 29:24–30:15; 52:14–25. This is because each species of living organism has its own sets of translocating enzymes, and there are "millions and millions" of species of living things on Earth. *Id*. at 29:24–30:15; 52:14–25. Translocating enzymes include proteins of widely varying structures, mechanisms, and functions. *See*, *e.g.*, Ex. V5, McHenry Tr. at 67:6–11; 68:21–69:1; 69:10–14; *see also* Ha Decl. at ¶ 154; Ex. V6, McHenry Reb. at ¶ 179. For example, one class of translocating enzymes are polymerases, which synthesize DNA. *See id.*; *see also* Ha Decl. at ¶ 154. Other classes of translocating enzymes include (but are not limited to) helicases, which unwind DNA, and exonucleases, which cut DNA. *See*, *e.g.*, Ex. V5, McHenry Tr. at 67:6–11; 68:21–69:1; 69:10–14; *see also* Ha Decl. at ¶ 154. Due to the vast structural, functional, and mechanistic differences between different classes of enzymes, knowledge and/or teachings about the properties of one class would not typically apply to other classes. *Id.* at ¶¶ 155-58; *see also id.* at ¶ 128.

The '056 Patent's specification contemplates that each of these many millions of translocating enzymes can be changed via mutation to satisfy the claims. '056 Patent at 29:19–29. Since most enzymes are hundreds of amino acids long and the amino acid at any position can be changed, there are "innumerable" combinations of possible mutations. *See* Ex. V6, McHenry Reb. at ¶ 290 [redacted] *see also* Ha Decl. at ¶ 154; '056 Patent at Table 1 [redacted]

Even if the sequence and structure of a translocating enzyme are known, each mutant has to be assessed individually to determine how it modifies the enzyme's behavior. Ex. V5, McHenry Tr. [redacted]

The '056 Patent's Asserted Claims (the "'056 Claims") purport to embrace every translocating enzyme and set of reaction conditions for that enzyme capable of performing the claimed nanopore sequencing method. *Id.* at 80:22–81:6. Thus, to identify the full scope of the '056 Claims, innumerable translocating enzymes would have to be individually tested to determine both their fitness for use in a nanopore sequencing system and the reaction conditions at which each enzyme would exhibit the claimed kinetic steps in a nanopore system.

b. ***The only reference the '056 Patent cites for nanopore sequencing reaction conditions does not use a translocating enzyme.***

The '056 Patent does not provide a single set of reaction conditions that would generate the claimed enzymatic profile and lacks any working examples related to the asserted claims. Ha Decl. at ¶ 162 ("[T]he '056 Patent does not provide any set of reaction conditions such that an enzyme would exhibit two kinetic steps in a nanopore sequencing system."); Ex. V5, McHenry Tr. at 92:21–25 ([redacted]). The only support the '056 Patent provides for nanopore sequencing using a translocating enzyme is a reference to a journal article by Hurt *et al*. Ex. V4,

'056 Patent at 36:4–13. However, both parties agree that this reference does not teach or provide any guidance as to the reaction conditions for a translocating enzyme in a nanopore system. *See* Ex. V6, McHenry Reb. at ¶ 202 ([redacted]); Ha Decl. at ¶ 138.

3. The '056 Claims are indefinite because a POSA can never be reasonably certain of claim scope.

A POSA can never be reasonably certain of the '056 Claims' scope—therefore, the '056 Claims are indefinite. *Nautilus,* 134 S. Ct. at 2119. The '056 Claims each require that "the translocating enzyme and the reaction conditions are selected such that the translocating enzyme exhibits two kinetic steps wherein each of the kinetic steps has a rate constant, and the ratio of the rate constants of the kinetic steps is from 10:1 to 1:10." D.I. 80-5; Ex. V4, '056 Patent at 58:44-67. But there are indeterminate numbers and types of steps in an enzymatic process, rendering it—as the Court previously found—impossible to determine with reasonable certainty the scope of the claim.[2] *See* D.I. 152 at 21.

The Court has since reconsidered its indefiniteness ruling, concluding both that, based on the record at the time that the '056 Claims "refer[] to a particular pair of 'two kinetic steps,'" but also that "the Court would benefit from further development of the record, including expert discovery." D.I. 255 at 5–6. Expert discovery is now complete, and PacBio has presented no evidence of how a POSA could identify that particular pair of two kinetic steps, because the term "exhibits" does not limit the '056 Claims. However, even if the '056 Claims were so limited, "kinetic steps" would still be indefinite because there necessarily remain an indeterminate number of those particular pairs of "exhibited" steps.

[2] ONT incorporates by reference its prior *Markman* briefing and oral argument on indefiniteness and all evidence submitted in support thereof. *See* D.I. 91.

a. *The plain and ordinary meaning of "exhibits" does not limit the term "kinetic steps."*

The plain and ordinary meaning of "exhibits" in the biochemical arts is "to possess a property." *See* Ha Decl. at ¶ 30. Nowhere does the '056 Patent provide an alternate definition. *See Thorner v. Sony Comput. Entm't Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012) ("To act as its own lexicographer, a patentee must 'clearly set forth a definition of the disputed claim term' other than its plain and ordinary meaning."). Thus, the '056 Claims must include ***every*** kinetic step that the enzyme possesses. And, because the number of kinetic steps is indeterminate, it is impossible for a POSA to determine with reasonable certainty the scope of the claim.

Unable to find a clear definition of "kinetic step," PacBio now argues that "exhibits" has a special meaning in the '056 Claims that renders "kinetic step" definite—that an "exhibit[ed]" step is one that affects the reaction's probability for residence time (henceforth "Dwell Time") distribution. *See* D.I. 156 at 7; *see also id*. at 4–5. But PacBio's own arguments demonstrate the circularity of this definition. For example, in prosecuting a continuation to the '056 Patent, PacBio argued that the "exhibit[ed]" steps ***in the '056 Patent*** are simply "observ***able***" steps.[3] Ex. V7, Interview Summary dated September 20, 2019 at 4. And, as '056 Patent inventor Dr. Stephen Turner has explained, [redacted] Ex. V8, Turner Tr. at 165:20–23 ([redacted]). Thus, by PacBio's own logic, exhibited steps are simply steps that can be assigned a rate constant. But PacBio also argued to this Court that the claimed "kinetic steps" are "reaction step[s] that can be associated with a rate constant." D.I. 91 at 16; *see also* D.I. 255 at 6 (explaining that defining "kinetic step" as "a reaction step that can be associated with a rate constant" is "not

[3] Notably, PacBio presents new claims in this continuation that attempt to avoid the '056 Claims' indefiniteness—PacBio now claims an enzyme that "exhibits two kinetically observable steps." *See* Ex. V7, Interview Summary dated September 20, 2019 at 4.

helpful in resolving the parties' dispute."). If "kinetic steps" and "exhibited steps" have the same definition, "exhibits" carries no special meaning as to the scope of "kinetic step," confirming that "kinetic steps" remains indefinite.

b. ***"Exhibit[ed]" kinetic steps could be based on an indeterminate number of Dwell Time curves, and thus would still be indefinite.***

In seeking reconsideration, PacBio argued that a POSA need not even identify two kinetic steps in the reaction mechanism in order to assess infringement,[4] and instead can find the "exhibit[ed]" steps by observing if the reaction's Dwell Time curve has a peaked distribution. D.I. 156 at 7. A POSA [redacted]. *See* Ex. V8, Turner Tr. at 170:13–25. In other words, the '056 Patent would be "referring to a particular pair of 'two kinetic steps'" that can be found by fitting the Dwell Time curve. D.I. 255 at 5. However, this definition necessarily requires each reaction to have a specific Dwell Time curve. The evidence shows that the pertinent reactions have an indeterminate number of Dwell Time curves and thus an indeterminate number of particular pairs—one for each Dwell Time curve—making it impossible to be certain of the '056 Claims' scope.

As Dr. Ha explains, a reaction can have multiple Dwell-Time curves. Ha Decl. at ¶ 74. For example, the authors of at least one reference relating to determining kinetic step rates with Dwell Time curves analyzed the same data two different ways: 1) they measured the time between the short spikes in the data, and 2) they measured the time between the long pauses in the data. *Id.* at ¶¶ 71–72. Each method measured a different step of the reaction. *Id.* at ¶ 72. Because each method measured a different step, each method generated a different curve from the exact same reaction—

[4] Of course, this interpretation ignores the '056 Claims' plain language, which defines the scope of the invention based on quantified rate constants of the recited steps.

one curve was exponential (Fig. 5a below), one curve was peaked (Fig. 4a below). *Id.* at ¶ 73.

There is an arbitrary number of different ways to process data, each one observing a different part of the reaction. *Id.* at ¶ 68. Therefore, it is impossible to know whether two steps will fall within the claimed ratio, as there will always be another method of processing the data. Thus, PacBio's new definition of "exhibits" does not cure the '056 Claims' defect. *Id.*

PacBio and its expert Dr. Charles McHenry recognize that a POSA can also assess infringement by simply comparing measured rate constants. *See* Ex. V9, PacBio's Infringement Contentions at 23–24; Ex. V10, McHenry Op. at ¶ 138. This is the method Dr. McHenry used to support his opinion that ONT's E7 enzyme infringed the '056 Claims. Ex. V10, McHenry Op. at ¶ 138; *see also* Ex. V9, PacBio's Infringement Contentions at 23–24. In that analysis, Dr. McHenry compared ONT's reported rate constants, determined that the rate constants [redacted], and on that basis opined that [redacted] indicates infringement. *See* Ex. V10, McHenry Op. at ¶ 138; *see also* Ex. V9, PacBio's Infringement Contentions at 23–24.

Showcasing the '056 Claims' indefiniteness, application of PacBio's Dwell-Time distribution infringement test to that same data indicates ***non***infringement. As noted, both PacBio and Dr. McHenry argue that single-exponential Dwell-Time distributions indicate ***non***infringement. Ex. V5, McHenry Tr. at 187:21–25 ([redacted]); D.I. 156 at 7 ([redacted]

[redacted]); *see also* Ex. V5, McHenry Tr. at 201:6–10 ([redacted]). ONT's [redacted]

Ex. V11, ONT_DEL00196028 at ONT_DEL00196037; *see also* Ex. V10, McHenry Op. at ¶ 138.

Thus, under PacBio's Dwell-Time distribution test, [redacted] D.I. 156 at 7. However, under PacBio's rate-constant measuring test, [redacted]. Ex. V9, PacBio's Infringement Contentions at 23–24. PacBio's different tests yield different results. *See Teva*, 789 F.3d at 1344–45 (claims indefinite because different methods of measuring the claimed polymer weight provided different results); *see also Dow Chem Co.*, 803 F.3d at 633-35.

Whether the Court defines "kinetic step" or "exhibits," the problem with the claims remains the same: there is an indefinite number of ways to observe the data, and it is therefore impossible to know if one of those ways will result in the [redacted] PacBio argues indicates infringement. *See Teva*, 789 F.3d at 1344–45; *Dow Chem Co.*, 803 F.3d at 633–35.

Since a POSA cannot be reasonably certain of the '056 Claims' scope, they are indefinite.

4. The '056 Claims are not enabled because undue experimentation would be required to practice their full scope.

The enablement requirement maintains the fundamental bargain at the heart of patent law: in

exchange for its monopoly, the patentee must commensurately enrich the "public knowledge." *Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1195–96 (Fed. Cir. 1999). But while the scope of the '056 Claims is very broad—encompassing any combination of translocating enzyme and reaction conditions that might exhibit the claimed steps—the '056 Patent does not "enrich" the public knowledge in a manner commensurate with that broad scope.[5]

Instead, PacBio's own expert admits that the '056 Patent merely provides a "layout of the variables that one would survey to get a working system." Ex. V5, McHenry Tr. at 87:2–4. The specification of the '056 Patent provides neither meaningful guidance toward compatible translocating enzymes, nor a single set of reaction conditions that would result in the claimed '056 process. Enablement requires more than providing "a starting point for further iterative research in an unpredictable and poorly understood field." *Wyeth*, 720 F.3d at 1386. And yet, as PacBio's expert acknowledges, that is all the '056's specification does. Ex. V5, McHenry Tr. at 87:2–4.

Because the *Wands* factors overwhelmingly show a POSA could not practice the full scope of the '056 Claims without undue experimentation, they are not enabled.

a. *The '056 Claims' scope is vast.*

There is no real dispute that the '056 Claims' scope is vast.[6] The '056 Claims include all combinations of enzymes and reaction conditions that achieve the claimed result. Even individually, the number of potential enzymes and the number of potential reaction conditions are both enormous—resulting in innumerable combinations of the two.

As described above, the '056 Claims include all translocating enzymes, regardless of structure. *See* Ex. V5, McHenry Tr. at 80:22–81:6. This means the '056 Claims—without accounting for

[5] *See infra* at § IV.A.4.

[6] *See supra* at § IV.A.2.a.

mutants—embrace many (many) millions of enzymes.[7] Accounting for mutants, Dr. Ha characterized the species encompassed by the '056 Claims as "innumerable." Ha Decl. at ¶ 154.

The '056 Claims are not just broad by sheer number of species; they also claim enzymes of entirely different structures, mechanisms, and functions *See*, *e.g.*, Ex. V5, McHenry Tr. at 67:6–11; 68:21–69:1; 69:10–14; *see also* Ha Decl. at ¶ 154. The fundamental differences across the spectrum of the numerous families of claimed translocating enzymes renders the claimed scope substantially more varied than similar claims that have been found non-enabled. *See Wyeth*, 720 F.3d at 1382–83 (claims directed to derivatives of a specific organic molecule); *Idenix Pharms. v. Gilead Scis.*, 2019 WL 5583543 at *2 (Fed. Cir. 2019) (claims directed to "nucleoside compounds having a specific chemical and stereochemical structure"); *MorphoSys v. Janssen Biotech, Inc.*, 358 F. Supp. 3d 354, 373 ("[T]he claims here are directed to a composition of matter genus that is claimed partially by the composition's structure and partially by its function.").

Not only do the '056 Claims encompass every translocating enzyme capable of performing the '056 method, but they also encompasses any and all such reaction conditions for those enzymes that result in the claimed process. Each enzyme will have its own required reaction conditions, and the '056 Claims constrain them only by result. *See* Ex. V5, McHenry Tr. at 98:10–19. Thus, there is similarly a near "infinite" number of possible reaction conditions. Ha Decl. at ¶ 167. This factor strongly supports a finding of undue experimentation.

b. *The nanopore sequencing art was nascent as of the priority date.*

PacBio also does not meaningfully dispute that nanopore sequencing was a nascent technology as of the '056 Patent's priority date, [redacted] *See*, *e.g.*, Ex. V8, Turner Tr. at 7:17–20; *see also* Ex. V12, Fehr Tr. at 147:8–14. In fact, both Dr. Ha (ONT's expert)

[7] *See supra* at § IV.A.2.a.

and Dr. Adrian Fehr (an inventor of the '056 Patent's grandparent) agree that normal DNA could not be sequenced as of the priority date. *See* Ha Decl. at ¶ 110 ("No-one had published successfully determining the sequence of a DNA strand using nanopore sequencing before 2010."); Ex. V12, Fehr Tr. at 148:1–6 ([redacted]).

Moreover, even if aspects of nanopore sequencing were known, Dr. McHenry, PacBio's expert, explained that the '056 Patent is directed to using a translocating protein to regulate nanopore translocation—a feat only reported in 2010. Ex. V6, McHenry Reb. at ¶ 307 ([redacted]) (quoting [redacted]); *see also* Ex. V6, McHenry Reb. at ¶ 298 ("A Person of Ordinary Skill would understand that the '056 Patent's specification is directed towards advantageous enzymes...."). This also strongly supports a finding of undue experimentation.

c. *Modifying enzymes and reaction conditions to achieve specific enzyme behavior was unpredictable.*

PacBio also does not meaningfully dispute that translocating enzyme behavior and the reaction conditions under which that translocating enzyme would exhibit the claimed behavior in a nanopore system were unpredictable as of the '056 Patent's priority date.[8]

Predicting and modifying enzyme behavior is unpredictable. *MorphoSys*, 358 F. Supp. 3d at 372 (antibody art is unpredictable since a "POSA would not be able to predict the function of these antibodies from their sequences," and therefore would require "screening" or "discovering the

[8] *See supra* at § IV.A.2.a. Biotechnology, including enzyme technology, is generally considered unpredictable. *See In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009).

antibodies *de novo*").[9] To find an enzyme that had reduced activity in a nanopore system, for example, Dr. McHenry agreed that a POSA would have to [redacted] Ex. V5, McHenry Tr. at 114:9–19; *see also id.* at 117:3–13 ([redacted]); 126:10–17 ([redacted]).

Moreover, even additional information about a translocating enzyme, such as its crystal structure, might not help;[10] Dr. McHenry explained that a crystal structure could lead researchers down a [redacted] and [redacted] Ex. V5, McHenry Tr. at 121:16–22. And if little information was known about an enzyme, a researcher would have to "[redacted] *Id.* at 116:7–11.

But mutating the enzyme is only half the story—once a suitable mutant is obtained, a POSA must still determine the reaction conditions that are capable of getting the mutant to exhibit the claimed two-step behavior in a nanopore system. Ha Decl. at ¶ 145. And, just like finding the right enzyme, Dr. McHenry agreed that a POSA would have to [redacted] Ex. V5, McHenry Tr. at 93:4–6; *see also id.* at 83:18–84:3 ([redacted]); 97–98

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[9] Enzyme engineering stands at the crossroads of chemical reaction and physiological activity, rendering it highly unpredictable. *See In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity); *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

[10] Dr. McHenry acknowledged t[redacted] *See* Ex. V5, McHenry Tr. at 25:10–14.

([redacted]); 100:23–101:13 ([redacted]). Thus, the level of unpredictability is high, supporting a finding of undue experimentation.

d. *Large amounts of experimentation would be needed to make or use the full scope of the '056 Patent's alleged invention.*

Because the scope of the '056 Claims is vast,[11] and enzyme behavior is unpredictable,[12] as Dr. McHenry explained, the different combinations of translocating enzyme and reaction conditions would have to be individually made and tested to find a combination both capable of and suitable for practicing the claims.[13] In essence, a POSA would have to perform a screen of screens—translocating enzyme mutants must be screened by testing each one in a screen of possible two-step reaction conditions. Thus, [redacted] Ex. V6, McHenry Reb. at ¶ 290; Ha Decl. at ¶ 127 ("I agree that making the mutants exhibiting two-step behavior would be laborious."); *but cf.* Ex. V5, McHenry Tr. at 103:12–15.

And, after that extensive trial-and-error screening, a POSA would still have to "make[] combinations" of the best mutants and iteratively re-screen to find enzymes capable of two-step behavior. *See id*. at 126:5–17 ([redacted]). A POSA would not even know how many iterations are required, because there is [redacted] the number of required mutations [redacted] *Id*. at 122:16–123:13.

Simply telling a POSA to search for the combination of translocating enzyme mutant and reaction conditions that happen to exhibit two-step behavior in a nanopore system is in no way enabling disclosure. *See Wyeth*, 720 F.3d at 1385 (no enablement where "practicing the full scope of

[11] *See supra* § IV.A.4.a.
[12] *See supra* § IV.A.4.c.
[13] *See supra* § IV.A.4.c.

the claims would require synthesizing and screening at least tens of thousands of compounds"); *MorphoSys*, 358 F. Supp. 3d at 372 (when "the claims recite functional limitations that cover countless embodiments in an unpredictable field, the specification must do more than place a POSA at 'a starting point... for further research' and instruct them to 'engage in an iterative, trial-and-error process.'") (quoting *ALZA*, 603 F.3d at 941); *In re '318 Patent Infringement Litig.*, 583 F.3d 1317, 1327 (Fed. Cir. 2009) ("[T]he specification, even read in the light of the knowledge of those skilled in the art, does no more than state a hypothesis and propose testing to determine the accuracy of that hypothesis. That is not sufficient."). The '056 Claims cover a near-infinite series of enzymes and reaction conditions, bounded only by functional limitations, which would have to be individually tested in an iterative, trial-and-error process. The volume of testing alone points to undue experimentation.

Finally, none of this screening even addresses the challenge of adapting enzymes to a nanopore system. Even though enzymatic control of DNA translocation through a nanopore had been theorized in the late 1990s, it was not reported until 2010. Ex. V13, Akeson Rep. at ¶ 36–37. This is because, among other reasons, most of the tested translocating enzymes "quickly fell off the DNA, only briefly moving the strand through the pore." *Id.* at ¶ 16. Solving this problem took "hundreds of hours of effort over several years"—well beyond routine screening. *Id.* In total, this also supports a finding of undue experimentation.

e. ***The '056 Patent provides no working examples or other meaningful guidance towards finding embodiments of its methods.***

The '056 Patent contains virtually no guidance as to: 1) what mutations to make in translocating enzymes to achieve two-step enzymes, 2) what reaction conditions to use with those enzymes, 3) how to screen the translocating enzymes and reaction conditions, or 4) how to adapt the reaction conditions used in the screen for a nanopore sequencing apparatus. And, despite the weak

guidance in such a highly unpredictable field, the '056 Patent does not provide a single working example for a POSA to use as a template.

The guidance toward developing two-step enzymes is scant at best and premised on experiments not performed with nanopore sequencing. Only mutants for a single enzyme are described—Φ29 polymerase—and, as to why different candidate mutants from Table 1 were combined to yield the 10 two-step Φ29 mutants described in Table 2, the specification provides no explanation. Because there's no evidence the mutants were tested in a nanopore system, Dr. McHenry was not even sure that the Φ29 mutants described in Table 2 could be used to practice the '056 claims. Ex. V5, McHenry Tr. at 136:7–13. At best, the Φ29 mutants described in the '056 Patent are an insufficient "starting point, a direction for further research." *Genentech*, 108 F.3d at 1366.

This deficiency is even greater for enzymes other than Φ29 polymerase. Other translocating enzymes, such as exonucleases and helicases, have [redacted] to polymerases like Φ29. *See, e.g.*, Ex. V5, McHenry Tr. at 67:6–11; 68:21–69:1; 69:10–14; *see also supra* at § IV.A.2.a. Despite that difference, the '056 Patent does not even ***suggest*** a single helicase or exonuclease to start with, let alone explain what modifications to make it. Thus, the '056 Patent provides ***no*** guidance for any translocating enzymes beyond that for a single polymerases.

Furthermore, the '056 Patent does not explain or provide any guidance on what reaction conditions to use with the 10 disclosed Φ29 mutants (or any other enzymes, for that matter), or even where a POSA should start looking. Instead, it merely provides a [redacted][14] *See* Ex. V5, McHenry Tr. at 87:2–4. Dr.

[14] In fact, the only guidance in the '056 Patent is the vague suggestion that some additives can slow some kinetic steps. *See* '056 Patent at 33:9–34:2 ("In some case[s], the addition of solvent can be used to change the rate of one or more steps in the polymerase reaction. For example, the

McHenry [redacted]. *Id.* at 91:19–23 ([redacted]). The presumed knowledge of one skilled in the art cannot provide this missing information, because those conditions are one of the supposedly-novel features of the '056 Claims. *Auto. Tech. Int'l, Inc. v. BMW of North Am., Inc.*, 501 F.3d 1274, 1283–84 (Fed. Cir. 2007) ("[W]hen there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required.") (quoting *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997)).

And, despite the necessity of screening to find enzymes and reaction conditions capable of practicing the claims, the '056 Patent does not explain how such screening should, could, or would be performed. In fact, the '056 Patent fails to describe how to perform nanopore sequencing. Given the nascence of the art, this does not approach the "reasonable amount of guidance" required for enablement. *Promega Corp. v. Life Techs. Corp.*, 773 F.3d 1338, 1349 (Fed. Cir. 2014).

Confounding things further, the '056 Patent does not explain how to adapt reaction conditions from other systems to nanopore reaction conditions. As Dr. Ha explained, "an enzyme used in a nanopore sequencing device is exposed to several unique stresses—for example, the nanopore system includes both a voltage, which not only affects the translocating enzyme but also pushes or pulls the DNA, and the nanopore itself, which can interact with both the translocating enzyme and the DNA, further affecting the kinetics. Each of these factors must be accounted for by the reaction conditions." Ha Decl. at ¶ 145. The '056 Patent is silent on this issue.

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solvent may slow one or more steps in the polymerase reaction."). Disregarding the low utility of such nebulous guidance, PacBio argues that ONT allegedly achieved two-step kinetics by speeding up the reaction. *See* McHenry Op. at ¶ 120. This means a POSA who invented a way to follow the '056 Patent's suggestions would still never stumble on ONT's method.

Finally, the '056 Patent provides ***no*** working examples of an enzyme exhibiting the claimed behavior in a nanopore. Ha Decl. at ¶ 162 ("[T]he '056 Patent does not provide any set of reaction conditions such that an enzyme would exhibit two kinetic steps in a nanopore sequencing system."); Ex. V5, McHenry Tr. at 92:21–25 ([redacted]). This means a POSA would have to do more work than the inventors of the '056 Patent to find variants of any enzyme other than Φ29—after all, a POSA would have to find both a working enzyme ***and*** reaction conditions. *See MorphoSys*, 358 F. Supp. 3d at 372 (finding the level of guidance "unhelpful" where "a POSA attempting to obtain a claimed antibody that is not a variant of a known antibody would have to do essentially the same amount of work as the inventors...."). At best, the specification is "a starting point for further iterative research in an unpredictable and poorly understood field," which is not an enabling disclosure. *Wyeth*, 720 F.3d at 1386.

"Where... the claimed invention is the application of an unpredictable technology in the early stages of development, an enabling description of the specification must provide those skilled in the art with a specific and useful teaching." *Genentech*, 108 F.3d at 1367–68 (claims to nascent cleavable fusion expression methods were not enabled because "the specification does not describe a specific material to be cleaved or any reaction conditions under which cleavable fusion expression would work"). As explained above, nanopore sequencing was a nascent technology in 2009.[15] Nowhere does the '056 Patent teach a POSA how to practice claim 1. Thus, the level of guidance provided in the '056 Patent is insufficient, weighing in favor of undue experimentation.

The factors above demonstrate that, even with the '056 Patent's disclosure, a POSA would need to conduct additional undue experimentation to identify an enzyme and reaction conditions that

[15] *See supra* at § IV.A.4.b.

would operate according to the '056 Claims. Thus, those claims are not enabled.

B. The [redacted] Algorithm Does Not Infringe the '400 and '323 Patents.

1. Legal Standard for Infringement

A defendant seeking summary judgment of non-infringement can simply point to the ways in which the accused products or methods fail to meet the claim limitations. *Exigent Tech., Inc. v. Atrana Solutions, Inc*., 442 F.3d 1301, 1309 (Fed. Cir. 2006). The burden of production then shifts to the patentee to "identify genuine issues that preclude summary judgment." *Optivus Tech., Inc. v. Ion Beam Applications S.A.*, 469 F.3d 978, 990 (Fed. Cir. 2006); *see Exigent Tech., Inc.* at 1308-09. A patentee must then provide concrete evidence, not conclusory expert opinion, to raise a genuine issue of material fact that infringement exists, either literally or under the doctrine of equivalents ("DOE"). *Arthur A. Collins, Inc. v. Northern Telecom Ltd.*, 216 F.3d 1042, 1046 (Fed. Cir. 2000). DOE analysis is conducted on a limitation by limitation basis and requires "special vigilance against allowing the concept of equivalence to eliminate completely any such elements." *Id.* at 40. "[T]he doctrine of equivalents, when applied broadly, conflicts with the definitional and public-notice functions of the statutory claiming requirement." *Id*. at 29; *see also Sage Prods., Inc. v. Devon Indus., Inc*., 126 F.3d 1420, 1425 (Fed. Cir. 1997) ("between the patentee who had a clear opportunity to negotiate broader claims but did not do so, and the public at large," the patentee "must bear the cost of its failure to seek protection for [a] foreseeable alteration").

2. Facts Relevant to the '400 and '323 Infringement Analysis

The accused products use basecalling software to determine the sequence of bases in a nucleic acid. Goldman Decl. at ¶ 8; Ex. V14, Dessimoz Op. at ¶ 184. Since May 14, 2019, [redacted]. Goldman Decl. at ¶ 9; Ex. V14, Dessimoz Op. at ¶¶ 57, 116. [redacted]

[redacted]. Goldman Decl. at ¶ 14. [redacted]. *Id.* at ¶ 10; Ex. V14, Dessimoz Op. at ¶ 196. [redacted]. Goldman Decl. at ¶ 14; Ex. V14, Dessimoz Op. at ¶ 198.

3. PacBio Has Produced No Evidence that Use of the [redacted] Algorithm Infringes the '400 and '323 Patents.

ONT is entitled to summary judgment of non-infringement of the '400 Patent and '323 Patents for the accused products that use ONT's [redacted] algorithm, because PacBio has not produced—and cannot produce—evidence that the algorithm practices each limitation of the asserted claims, either literally or under the doctrine of equivalents. Goldman Decl. at ¶ 12. Beyond conclusory statements that conflate the [redacted] algorithm with other accused basecalling algorithms, PacBio has failed to provide any concrete evidence of infringement specific to the [redacted] algorithm. Indeed, PacBio does not even advance a specific infringement theory—literal or under DOE—for the [redacted] algorithm. A patentee, however, must provide concrete evidence, not conclusory expert opinion, to raise a genuine issue of material fact that infringement exists. *Arthur A. Collins, Inc. v. Northern Telecom Ltd.*, 216 F.3d 1042, 1046 (Fed. Cir. 2000).

According to PacBio's expert Dr. Christophe Dessimoz, [redacted] Ex. V14,

Dessimoz Op. at ¶¶ 35-37. [redacted] *Id*. The asserted claim(s) specifically recite "*(c) measuring a property which has a value that varies for N monomeric units of the template nucleic acid in the pore*" and "*d) determining the sequence of the template nucleic acid using the measured property from step (c) by performing a process including comparing the measured property / electrical signal from step (c) to calibration information produced by measuring such property for [each of the] 4 to the N sequence combinations / that accounts for the electrical signal for 4 to the N sequence combinations"* limitation(s), as required by the '400 and '323 claims. '400 Patent at cl. 1; '323 Patent at cl. 1; D.I. 153 at 2. Put simply, the claims are directed to *a method for determining the sequence of a template nucleic acid by comparing a measured current, wherein the current varies for N monomeric units of the template in the pore, to calibration information produced by measuring or accounting for the current value for each of the 4^N sequence combinations*. Ex. V14, Dessimoz Op. at ¶ 183; *see also* Ex. V1, '400 Patent at cl. 1, Ex. V2, '323 Patent at cl. 1. The claim language makes clear that both the measured and calibrated current values are functions of N monomeric units—*i.e.*, N-mer[16]—and the measured current value from a template nucleic acid is compared to the calibrated current values to determine the sequence of the template nucleic acid.

a. *The [redacted] Algorithm Does Not Use the Claimed "Calibration Information" or "Compare" Such Information as Required by the Asserted Claims of the '400 and '323 Patents.*

There is no evidence that the [redacted] algorithm has or uses calibration information produced by measuring such property [current] for each of the 4 to the N sequence combinations or calibration information that accounts for the electrical signal [current] for each of the 4 to the

[16] While the parties dispute the value of "N" in the ONT products, and relatedly whether N is determined based on a single current measurement, that dispute has no bearing on this motion.

N sequence combinations. As Dr. Goldman has explained, the [redacted] algorithm represents a paradigm shift from previous algorithms used by ONT; [redacted]. Goldman Decl. at ¶ 14. Dr. Dessimoz has asserted that ONT [redacted][17] and ONT's [redacted] Ex. V14, Dessimoz Op. at ¶¶ 107, 112. But the evidence Dr. Dessimoz cites in support of these statements all relates to ONT's [redacted]—not the [redacted]. *Id.* Dr. Dessimoz does not point to anything in the [redacted] algorithm that actually models any process based on [redacted]. In fact, Dr. Goldman has expressly pointed out that in [redacted] Goldman Decl. at ¶ 14. Even [redacted] *Id.* at ¶¶ 14-15. Accordingly, Dr. Dessimoz has not provided any evidence to show that ONT's products using the [redacted] algorithm use calibration information produced by measuring, calculating or experimentally determining current signals corresponding to each of the 4^N possible combinations of nucleotides. *Id.* at ¶ 13. Indeed, in Dr. Goldman's opinion, [redacted] *Id.*

Dr. Dessimoz asserts that because the [redacted] that is [redacted] includes [redacted] it has calibration information produced by measuring such property for each of the 4 to the N sequence combinations. Ex. V14, Dessimoz Op. at ¶¶ 200-201. However, as Dr. Goldman has explained, even if its training data set includes all 4^N different combinations of N

[17] While ONT disagrees that [redacted] refers to the set of bases that affect the signal in the nanopore, that dispute is not relevant to this motion.

nucleotides (which ONT does not concede), this does not itself provide evidence that the [redacted] learns that particular [redacted], or that the [redacted] accounts for that particular [redacted], or generates calibration information produced by measuring, calculating or experimentally determining current signals corresponding to each of the 4^N possible combinations of nucleotides. Goldman Decl. at ¶ 15. To the contrary, [redacted]. *Id.*

Indeed, Dr. Dessimoz acknowledges that the [redacted] algorithm does not have the [redacted] construct. Ex. V14, Dessimoz Op. at ¶ 116 ([redacted]). Further, Dr. Dessimoz acknowledges that the architecture of the [redacted] algorithm does not allow for calibration information produced by measuring or accounting for the current value for each of the 4^N sequence combinations. Specifically, Dr. Dessimoz acknowledges that [redacted] as shown in the figure below. *Id.* at ¶ 117.

[redacted]

As shown, the output space in the [redacted] algorithm is limited to [redacted] states, unlike the [redacted] or

[redacted] states in ONT's previous algorithms. Goldman Decl. at ¶ 17. If output space were an indication of the value of claimed "N" for a nanopore system—which it is not—then the value of "N" for [redacted] would be less than 3 (because 4^3 equals 64) and thus outside the Court's construction. Dr. Dessimoz even concedes that the output space in [redacted] is not consistent with his assertion that N is equal to [redacted] in ONT's accused products. Ex. V15, Dessimoz Tr. at 192:12-16. Specifically, he states: [redacted] *Id.*

Unable to find any [redacted] construct —let alone the claimed N-mer construct— in the [redacted] algorithm, Dr. Dessimoz assumes that [redacted] must use [redacted] of length equal to [redacted]. Ex. V14, Dessimoz Op. at ¶¶ 116-118. But even on summary judgment, it is *PacBio's* burden, not ONT's, to show that [redacted] does not differ in any relevant way from the previous algorithms used in the accused products. *See, e.g.*, *L & W, Inc. v. Shertech, Inc.*, 471 F.3d 1311, 1317 (Fed. Cir. 2006) ("[plaintiff] cannot simply 'assume' that all [accused] products are like the one [plaintiff's expert] tested and thereby shift to [defendant] the burden to show that is not the case."); *Out RAGE, LLC v. New Archery Prod. Corp.*, 2013 WL 12234188, at *19 (W.D. Wis. June 25, 2013) (granting summary judgment of non-infringement as to versions of the accused product that plaintiff's expert mentioned in his expert report, but did not independently analyze); *Alloc, Inc. v. Pergo, L.L.C.*, 751 F. Supp. 2d 1049, 1059 (E.D. Wis. 2010) (granting summary judgment of non-infringement as to 21 of 24 accused products where plaintiff presented no evidence "indicating how the testing of only three products provides evidence of infringement for the remaining, untested products"); *cf. Riverbed Tech., Inc. v. Silver Peak Sys., Inc.*, 2014 WL 266303, at *4 (D. Del. Jan. 24, 2014) (finding expert's analysis of single version of code to show infringement by multiple versions was proper where expert actually reviewed all applicable versions to determine the code

had not materially changed).

Indeed, Dr. Dessimoz cannot possibly show that the [redacted] algorithm has the [redacted] construct. Goldman Decl. at ¶ 13. Giving the [redacted] algorithm as an example, Dr. Dessimoz speculates that he would find infringement in a system even where the data structure [redacted] but if he could somehow surmise that it was designed that way only [redacted] Ex. V15, Dessimoz Tr. at 192:2 – 193:5. Even if Dr. Dessimoz had any evidence to support such speculation (he does not), he cannot opine that the [redacted] algorithm infringes the '400 and '323 Claims based simply on non-technical conjecture while maintaining that it [redacted] *Id.*

Nor has PacBio presented any evidence that the [redacted] algorithm compares the measured property (current) that varies for N monomeric units of the nucleic acid in the pore to the calibration information that is produced by measuring or accounts for all 4^N sequence combinations. Goldman Decl. at ¶ 16. Dr. Dessimoz asserts, without pointing to any evidence in the [redacted] algorithm, that [redacted] and [redacted] Ex. V14, Dessimoz Op. at ¶190. Even accepting Dr. Dessimoz's assumption that the [redacted],[18] there is no evidence that the [redacted] algorithm compares measured current values to any such calibration information as the '400 and '323 Claims require. *See* Goldman Decl. at ¶ 16. Dr. Dessimoz simply

[18] To the contrary, as noted above, Dr. Goldman explains that the training data that PacBio asserts to be the claimed "calibration information" is not itself present in the [redacted] algorithm code used to perform basecalls. Goldman Decl. at ¶¶ 13-16. Thus, it does not necessarily follow that the [redacted] algorithm uses that calibration information at all when it determines the sequence of a nucleic acid.

concludes that because the Taiyaki training data set includes the calibration information—which it does not—the [redacted] algorithm must "use" it for the claimed comparison. Ex. V14, Dessimoz Op. at ¶199. However, PacBio must provide concrete evidence, not conclusory expert opinion, to raise a genuine issue of material fact that infringement exists. *Arthur A. Collins, Inc. v. Northern Telecom Ltd.*, 216 F.3d 1042, 1046 (Fed. Cir. 2000).

b. *The [redacted] Algorithm Does Not Infringe the '400 and '323 Patents Under the Doctrine of Equivalents.*

Similar to its lack of literal infringement evidence, PacBio fails to put forward any specific evidence of how the [redacted] algorithm would perform step 1(d) of the '400 and '323 Claims under the doctrine of equivalents. Goldman Decl. at ¶ 12. Dr. Dessimoz's mere assertion that all of ONT's basecalling algorithms (including [redacted]) are based on use of recurrent neural networks, and assumption that all such [redacted] work the same way, cannot support infringement under DOE. *See Am. Calcar, Inc. v. Am. Honda Motor Co., Inc.*, 651 F.3d 1318, 1338 (Fed. Cir. 2011) ("essential inquiry" is whether accused product contains elements "equivalent to each claim element"); *Apeldyn Corp. v. AU Optronics Corp.*, 831 F. Supp. 2d 837, 843 (D. Del. 2011) (patentee's expert "does not provide the limitation-by-limitation discussion of equivalence"); *see also L & W, Inc. v. Shertech, Inc.,* 471 F.3d 1311, 1317 (Fed. Cir. 2006) ("[plaintiff] cannot simply 'assume' that all [accused] products are like the one [plaintiff's expert] tested and thereby shift to [defendant] the burden to show that is not the case."). Dr. Dessimoz's DOE analysis says nothing about how the [redacted] algorithm actually operates or uses any of the alleged calibration information (either in its training or in basecalling), much less does it describe how that operation is substantially the same as the "determining" and "comparing" steps of the '400 and '323 Claims.

The only expert who has performed this analysis – Dr. Goldman – concludes that the

[redacted] algorithm does not meet these requirements. Goldman Decl. at ¶ 20. As Dr. Goldman notes, the [redacted] algorithm does not operate in the same way as the claimed method of the '400 and '323 claims because that algorithm [redacted] let alone on the claimed N-mers or 4^N possible sequence combinations. *See id.* at ¶ 14. Dr. Goldman also notes the [redacted] algorithm is trained to minimize error function over the whole training data set, not necessarily to account for all sequences in that set, much less the 4^N sequence combinations required in the '400 and '323 Claims. *Id.* at ¶ 15. In addition, [redacted] transitions-based algorithm also results in improved accuracy in sequencing of homopolymers (*e.g.*, a series of repeating bases within a nucleic acid), and only allowing specific transitions between those representations, as shown in the very ONT document on which Dr. Dessimoz relies (reproduced below). Ex. V14, Dessimoz Op. at ¶ 116.

Dr. Dessimoz ignores these different results achieved by the [redacted] algorithm. Since the [redacted] algorithm operates in a substantially different way and can achieve substantially different results from the methods of the '400 and '323 Patents, it cannot infringe those claims under DOE. *See* Goldman Decl. at ¶ 20.

Moreover, based on PacBio's own representations before the USPTO, a POSA would understand that the [redacted] algorithm's approach is not interchangeable with the claimed methods of the '400 and '323 Claims. *Id.* at ¶¶ 18-20. It is undisputed that the Hibbs prior art describes methods for determining the sequence of a polynucleotide using a nanopore system in which at least 5 nucleotides contributed to the signal, and describes comparing that signal to "calibrated values" for at least some of the possible combinations of N monomeric units contributing to the signal. *Id.* at ¶ 28. In distinguishing step 1(d) of the '400 Claims following rejections over Hibbs in prosecution, PacBio added the calibration information and "comparing" elements to that step, and specifically argued that "in order to obtain reliable sequence information, one first has to understand how many bases within the pore are contributing to the signal (N)," and then "4 to the power N calibration measurements must be carried out to produce calibration information for sequence determination." *See* Goldman Decl. at ¶ 19. PacBio further argued that "[n]ot only does Hibbs et al. not describe the instant invention, but it actually teaches away from the invention because it instructs the researcher to only measure a small subset of the 4 to the N sequencing combinations of the instant method." *See also* Goldman Decl. at ¶ 19. In distinguishing step 1(d) of the '323 Claims from Hibbs, PacBio made virtually identical arguments, and further distinguished the claimed "comparing" step: "[n]ot only is carrying out the additional calibration experiments extra work, but ***having to compare the measured property to a larger number of values during sequencing*** is computationally more challenging" than the method of Hibbs. D.I. 80-8, '323 History (6/29/2017 Response) (emphasis added). Having distinguished Hibbs based on allegedly failing to disclose calibration information accounting for each of the all 4^N combinations and comparing a measured property to such combinations, PacBio cannot simply assert that algorithms lacking any [redacted] or N-mer construct whatsoever are "interchangeable" with the '400 and '323 Claims. Goldman Decl. at ¶¶ 18-20.

Accordingly, the accused products that use the [redacted] algorithm do not infringe the '400 and '323 Patents as a matter of law.

C. PacBio Has Produced No Evidence that Anyone Used ONT's [redacted] Product(s) to Practice the Methods of the '929 Patent in the U.S.

It is black letter law that "a method or process claim is directly infringed only when the process is performed." *Joy Techs., Inc. v. Flakt, Inc.*, 6 F.3d 770, 773-74 (Fed. Cir. 1993). The claims of the '929 Patent are method claims. PacBio generally alleges in its Fourth Amended Complaint (D.I. 299, Ex. D at ¶¶ 22, 60) that the use of ONT's [redacted] kits, in combination with the relevant accused devices, flow cells, and software, infringe the '929 claims. Yet, the only [redacted] kit PacBio has accused is the Native Barcoding Kit 2D (model number EXP-NBD203). Ex. V14, Dessimoz Op. at ¶ 66. PacBio has produced no evidence that ONT or its customers have used EXP-NBD203 to practice the methods claimed in the '929 Patent in the U.S.,[19] nor could it. As indicated in Dr. Hrdlicka's Expert Report (Ex. V16, Hrd. Op. at ¶ 41) and stated in the Dokos Declaration (Dokos Decl.), ONT never imported into the U.S. EXP-NBD203, nor has ONT ever made, sold, offered for sale, licensed, or otherwise supplied within the U.S. EXP-NBD203. Dokos Decl. at ¶¶ 2-4. It is undisputed that without EXP-NBD203, there is no combination of accused devices, flow cells, kits, and software, that can be used to practice the [redacted] that PacBio alleges is within the '929 claim scope. *See* Ex. V14, Dessimoz Op. at ¶¶ 65-66. Thus, there is no factual basis for PacBio's claim that ONT or its customers directly infringe the '929 Patent through "use" of any [redacted] product.

Absent proof of direct infringement, PacBio's allegations of indirect infringement as they relate to ONT's [redacted] also fail. *Joy Techs.*, 6 F.3d at 774 ("Liability for either active

[19] PacBio did not claim any damages resulting from any alleged use of ONT's [redacted] product(s) in the Prowse Expert Report (Ex. V17, Prowse Op.). Dr. Prowse also testified [redacted] Ex. V17, Prowse Op. at 205:3-10.

inducement of infringement or for contributory infringement is dependent upon the existence of direct infringement."). ONT is therefore entitled to summary judgment on PacBio's claims of direct and indirect infringement of the '929 Patent as they relate to ONT's [redacted]. *See* Fourth Amended Complaint (D.I. 299, Ex. D at Count II).

D. Winters-Hilt Grant, Akeson Grant, and their progress reports were publicly available before the April 10, 2009 priority date of the '400 and '323 Patents.

"[P]ublic accessibility has been called the touchstone in determining whether a reference constitutes a printed publication." *Kyocera Wireless Corp. v. Int'l Trade Comm'n*, 545 F.3d 1340, 1350 (Fed. Cir. 2008). A reference is publicly accessible if it "has been disseminated or otherwise made available to the extent persons interested and ordinary skilled in the subject matter or art exercising reasonable diligence can locate it." *Id*. Eligibility as a printed publication is a question of law based on underlying facts. *Id*.

The Winters-Hilt Grant and Akeson Grant are grant proposals made to the National Institutes of Health ("NIH") for research funds by Dr. Stephen Winters-Hilt and Dr. Mark Akeson. As attested by Dr. Sylvia Hall-Ellis, the NIH made project data and abstracts for such grant proposals available through an online database, which was indexed by Application ID, Grant Number, Project Title, Principal Investigator, and Abstract and supported the use of search terms. This database was updated with newly-funded grants weekly, so project data was publicly available within 7 to 10 days of funding. Hall-Ellis Decl. at ¶ 5. Furthermore, funded grant proposals were available under FOIA, and the information required to reasonably describe a funded grant proposal for FOIA purposes was available in this database. *Id.* at ¶ 6. Therefore, a funded grant proposal was publicly available under FOIA when its project data became publicly available (*i.e.*, within 7 to 10 days of funding). *Id.* Grant Number 1K22LM008794-01 to Stephen Winters-Hilt ("Winters-Hilt Grant") and its progress reports, Grant Numbers 1R21GM073617-02 and 1R21GM073617-03, were funded on September

15, 2005, September 15, 2006, and September 15, 2007, respectively. *Id.* at ¶¶ 7-8. Similarly, Grant Number 1R21GM073617-01A1 to Mark Akeson ("Akeson Grant") and its progress reports, Grant Numbers 1R21GM073617-02 and 1R21GM073617-03, were funded on April 1 of 2006, 2007, and 2008, respectively. *Id.* at ¶ 9-10. All of these facts are undisputed,[20] and clearly meet the standard for public availability.[21]

Therefore, because Winters-Hilt Grant, Akeson Grant, and their progress reports were publicly available before the April 10, 2009 priority date of the '400 and '323 Patents and qualify as prior art printed publications under 35 U.S.C. § 102, summary judgment is appropriate.

V. CONCLUSION

For the reasons stated above, the Court should enter summary judgment that (i) the '056 Patent is invalid as indefinite or lacking enablement; (ii) the accused products do not infringe the '400 and '323 Patents to the extent they use the [redacted] algorithm, (iii) ONT's [redacted] has not infringed the '929 Patent, and (iv) the Winters-Hilt Grant, the Akeson Grant, and their respective progress reports were publicly available as prior art under 35 U.S.C. § 102.

[20] ONT offered the declarant for a deposition but PacBio opted not to depose her.

[21] ONT requested that PacBio stipulate to the public availability of Winters-Hilt Grant and Akeson Grant or, alternatively, their abstracts, but PacBio declined to do so.

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November 22, 2019

CERTIFICATE OF SERVICE

I hereby certify that on November 22, 2019, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

I further certify that I caused copies of the foregoing document to be served on November 22, 2019, upon the following in the manner indicated:

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